

REMARKS/ARGUMENTS

Claims 23, 24 and 31-41 are pending in the application. Claims 23, 24 and 37 have been amended to clarify certain embodiments of the presently claimed invention. No new matter has been added. Reconsideration and withdrawal of the rejections in this application are respectfully requested.

I. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 23, 24 and 31-41 are rejected under 35 U.S.C. § 103(a) (“Section 103(a)”) as allegedly being obvious over U.S. Patent No. 5,998,457 to Kaddurah-Daouk (hereinafter “Kaddurah-Daouk”) in view of U.S. Patent No. 4,772,591 to Meisner (hereinafter “Meisner”), U.S. Patent No. 5,888,553 to Grant *et al.* (hereinafter “Grant”), U.S. Patent No. 5,756,469 to Beale (hereinafter “Beale ‘469”), and U.S. Patent No. 5,716,926 to Beale (hereinafter “Beale ‘926”). For the following reasons, Applicants disagree.

A. The Legal Standard

A finding of obviousness requires that “the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” 35 U.S.C. § 103(a). In its recent decision addressing the issue of obviousness, *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 U.S.P.Q.2d 1385 (2007), the Supreme Court stated that the following factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966) still control an obviousness inquiry: (1) the scope and content of the prior art; (2) the differences between the prior art and the claimed invention; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *KSR*, 127 S.Ct. at 1734 (quoting *Graham*); *see also* Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, Federal Register, Vol. 72, No. 195, October 10, 2007, pages 57527-57528. The Supreme Court also stated that it is “important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does....” *KSR*, 127 S.Ct. at 1741.

A *prima facie* case of obviousness can be established by showing a suggestion or motivation, either in the references themselves or in the knowledge generally available to one

of ordinary skill in the art, to modify the reference *and* to carry out the modification with a reasonable expectation of success, viewed in light of the prior art. Both the suggestion and the reasonable expectation of success must both be found in the prior art and *not* be based on the applicant's disclosure. *In re Dow Chemical Co.*, 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988).

With regard to the final point, the Supreme Court in *KSR* citing *Graham*, upheld the principle of *avoiding hindsight bias* and cautioned courts to *guard against reading into the prior art the teachings of the invention in issue*. *KSR*, 127 S. Ct. at 1742. Thus, the principles set forth in *Graham* and in *Dow Chemical* – which are still good law post-*KSR* – require that *both* the suggestion and the expectation of success must be found in the prior art, and not from knowledge gained from the applicant's disclosure.

Further, an Examiner may not rely on inherency to support an obviousness rejection. That “which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.” *In re Spormann*, 363 F.2d 444, 448, 150 U.S.P.Q. 449, 452 (C.C.P.A. 1966).

B. The Claims Are Not Obvious Over Kaddurah-Daouk In View Of Meisner, Grant, Beale '469 And Beale '926

As a preliminary matter, claims 24 and 37 have been amended to recite that the method is for accelerating healing in a subject having a defect in bone tissue caused by trauma or surgery.

In the Office Action (page 3, ¶1), the Examiner acknowledges that “Kaddurah-Daouk does not teach expressly the employment of creatine pyruvate for the treatment, or the particular amount administered, or the method may be employed for promoting growth and mineralization of bone; improving acceptance and osseous integration of bone; or accelerating healing, or the purity required as herein required.” However, on page 3, paragraph number 2, lines 14-17, the Examiner contends that, in view of Meisner, Grant, Beale '469, and Beale '926, “it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to employ creatine pyruvate composition, for improving bone conditions, or for accelerating healing of pathogenic bone conditions, including bone implantation and bone defect caused by trauma or otherwise.”

Applicants respectfully disagree with the Examiner for the following reasons:

First, Applicants submit that the cited references do not teach or suggest all limitations of the claimed methods. In particular, none of the references, either alone or together, ever mentions creatine pyruvate or an analogue thereof, much less teach or suggest administering creatine pyruvate or an analogue thereof to *a subject having a bone implant*, as recited in claim 23, or *a subject having a defect in bone tissue caused by trauma or surgery*, as recited in claims 24 and 37. The references' silence as to the administration of creatine pyruvate or analogue and the recited patient populations cannot be used as a basis for a Section 103(a) rejection, since "obviousness cannot be predicated on what is unknown." *In re Spormann*, 363 F.2d at 448.

Second, the references are directed to different classes of substance having different biochemical properties and for treating different diseases. For example, Kaddurah-Dauok discloses the use of a creatine compound for treating or preventing a metabolic disorder related to body weight control such as obesity and its associated diseases; Meisner discloses the use of a composition comprising, *inter alia*, creatine as an anti-inflammatory substance for promoting connective tissue growth and thus wound healing; Grant discloses the use of a non-steroidal anabolic composition, *optionally* containing creatine, for the building and sustaining of muscle mass; Beale '469 discloses the use of pyruvate and a cortisol blocker for increasing lean body mass or muscle tissue; and Beale '926 discloses the use of pyruvate and an anabolic protein composition for increasing lean body mass or muscle tissue. While some of the references allude to the treatment of osteoporosis, osteoarthritis or periodontitis, Applicants submit that these diseases do not necessarily relate to acceptance and osseous integration of a bone implant, as recited in claim 23, or are necessarily a bone defect caused by trauma or surgery, as recited in claims 24 and 37.

There is clearly no indication in the cited references that the creatine compound of Kaddurah-Dauok, Meisner and (optionally used in) Grant can be combined specifically with the pyruvate of Beale '469 and Beale '926 to produce creatine pyruvate for improving acceptance and osseous integration of a bone implant or for accelerating healing of a bone defect, as recited in claims 23 and amended claims 24 and 37, respectively. In fact, without Applicants' disclosure, the problems that are solved by the presently claimed invention are not even defined by any of the cited references. Thus, the ordinarily skilled person could not have combined the compounds of Kaddurah-Dauok, Meisner, Grant, Beale '469 and Beale '926 to arrive at the claimed methods.

Moreover, there is no teachings in each of the references to suggest a combination or substitution of compounds and therapeutic effects to arrive at the claimed invention. In particular, Kaddurah-Dauok's method requires the use of a compound which modules one or more of the structural or functional components of the creatine kinase/creatine phosphate system (see col. 2, lines 32-40). A person of ordinary skill in the art would not expect the composition of Meisner, which comprises a source of biologically active calcium, ascorbic acid, a precursor or stimulant of epinephrine or nor-epinephrine production, and a mild anti-inflammatory substance; the non-steroidal anabolic composition of Grant; the synergistic pyruvate/cortisol blocker composition of Beale '469; and the synergistic pyruvate/anabolic protein composition of Beale '926 to be freely interchangeable with Kaddurah-Dauok's creatine compound, since Kaddurah-Dauok's creatine compound and Meisner's composition, Grant's composition, and Beale '469 and Beale '926's synergistic compositions have different structural and functional properties. Thus, there is no guidance in the cited references and there are numerous combinations of the different substances within each composition. The person of ordinary skill in the art would find the results of combining different substances each for obtaining different therapeutic results highly unpredictable.

In addition, there is no indication in Meisner or Grant that creatine alone is effective for the desired therapy. Nor is there any indication in Beale '469 and Beale '926 that pyruvate alone is therapeutically effective, especially when the teachings stress the synergistic effect of pyruvate in combination with cortisol blocker (Beale '469) or an anabolic protein composition (Beale '926). Contrary to the Examiner's allegation, a person of ordinary skill in the art would not know that pyruvate alone or in combination with creatine would be useful for improving bone conditions.

Furthermore, Applicants submit that the teachings of Kaddurah-Dauok are complete for their intended purposes and, thus, a person of ordinary skill in the art would have no motivation to use a secondary reference, i.e., one of Meisner, Grant, Beale '469, and Beale '926, let alone multiple references, to modify the teachings of Kaddurah-Dauok. *In re Herschler*, 591 F.2d 693, 200 U.S.P.Q. 711 (C.C.P.A. 1979)¹. The Examiner's use of five

¹ The Court of Customs and Patent Appeals addressed a similar situation in *In re Herschler*, 591 F.2d 693, 200 U.S.P.Q. 711 (C.C.P.A. 1979), when it held that the Board had wrongly rejected the appealed claims as obvious. In *In re Herschler*, the applicant taught the use of dimethyl sulfoxide (DMSO) to enhance transdermal penetration of a number of

disparate references from which to pick and choose isolated disclosures without regard to the reference as a whole is indicated of hindsight reconstruction based on knowledge gained from the Applicant's disclosure. In particular, Applicants respectfully submit that hindsight reconstruction has been used in the rejection of the present invention to combine a metabolic disorder treatment (Kaddurah-Dauok) with a wound healing therapy (Meisner) and a body building regimen (Grant, Beale '469, and Beale '926). Such hindsight, however, is improper and should be avoided in determining obviousness. *See KSR*, 127 S. Ct. at 1742.

For the foregoing reasons, Applicants submit that a *prima facie* case of obviousness cannot be established based on the cited references. Accordingly, Applicants respectfully request that the Section 103(a) rejections be withdrawn.

compounds, and claimed the process of applying to the skin a mixture comprising DMSO and a physiologically active steroid. 591 F.2d at 695, 200 U.S.P.Q. at 712. The Board rejected the claims as obvious over a primary reference (the Lubowe patent), which disclosed a hair lotion containing an estrogenic hormone and a solubilizing agent other than DMSO, combined with a secondary reference (Faust), which taught that DMSO is a safe and effective solubilizing agent for cosmetic or dermatologic use. The CCPA reversed the Board's rejection on the grounds that disclosure of the primary reference was already complete for its intended purpose, so that one of ordinary skill in the art would not have been motivated to use the DMSO of the secondary reference.

Similar to the Lubowe patent, the disclosure of Kaddurah-Dauok is complete for its intended purpose, namely the use of a creatine compound for treating or preventing a metabolic disorder related to body weight control such as obesity and its associated diseases. Because the solution is complete, Kaddurah-Dauok provides no reason to look to the art for alternative solutions, and, in particular, no motivation to look to the pyruvate of Beale '469 or Beale '926, especially when the teachings of Beale '469 and Beale '926 relate to muscle building, and not bone implant or bone defect caused by trauma or surgery.

CONCLUSION

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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